

Spinal anesthesia in the parturient with multiple sclerosis : case discussion and literature review

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Abstract : A 30-year old female patient with a history of relapsing-remitting multiple sclerosis (MS) was planned for an elective cesarean section. Additionally, the patient suffered from Generalized Anxiety Disorder. After careful discussion with the patient, spinal anesthesia was chosen for the procedure. The anesthetic course was uneventful and cesarean section was without incident. No per- or post-operative complications were observed. No relapse or disease aggravation occurred in the first three months following delivery.

Subsequently, a more profound MEDLINE and EMBASE literature search was conducted to review current evidence regarding safety of neuraxial anesthesia, and more specifically spinal anesthesia, in patients with MS. Neuraxial anesthesia has historically always faced considerable skepticism in this population. Current consensus, however, postulates no contra-indication for the use of neuraxial anesthesia in patients with MS. Epidural anesthesia remains the conventional neuraxial technique for purely paradigmatic reasons. A number of cases may nowadays safely benefit from a spinal technique.

Keywords : Cesarean section ; spinal anesthesia ; epidural anesthesia ; multiple sclerosis

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory disease characterized by demyelination of the central nervous system (CNS), leading to incremental neural tissue injury over time. Presentation is diverse and determined by the affected nerve fibers (1, 2). White matter lesions on Magnetic Resonance Imaging (MRI) and analysis of cerebrospinal fluid can further support the diagnosis of MS. Etiology remains unclear. A well-supported theory is that environmental exposures, such as viral infections, can induce the disease in individuals that are genetically susceptible (3). There are several types of MS and each is characterized by a specific pattern of progression. Primary progressive MS is characterized by the absence of remission after initial presentation of symptoms with subsequent gradual progression of disability, while secondary

progressive MS starts as relapsing-remitting MS that evolves in progressive neurologic decline without periods of significant remission (2). About 90% of MS patients suffer from the relapsing-remitting type. Relapse episodes are largely unpredictable, although multiple risk factors have been described. These include infections, delivery and the post-partum period, stress, smoking, fatigue, and fever (4). Pregnancy is thought to protect against relapse, while the post-partum period is known to increase the risk for relapse (5). Incidence in Western Europe has been reported around 1/1000, but varies worldwide. Especially young female adults are affected, with an average onset age of 31 years and a female to male ratio around 2 (6-8). Treatment options are limited. The intended outcome is to reduce attack frequency and duration, and to provide symptom relief.

Since MS is one of the most common neurological diseases in young female adults, many anesthesiologists will be confronted with the anesthetic management for delivery in a parturient MS patient (9). Choosing the optimal anesthetic technique can be challenging, especially in view of concern for disease aggravation or relapse when using neuraxial techniques in this population. But is this concern justified? We will discuss anesthetic management options for delivery in patients with MS.

Emphasis will be on current evidence regarding safety of spinal anesthesia in patients with MS set for delivery. A literature search was conducted

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using the MEDLINE and EMBASE databases. References and citations were analyzed for other applicable studies. Search terms included the words “Spinal Anesthesia” OR “Epidural Anesthesia” OR “Cesarean Section” AND “Multiple Sclerosis”. No restrictions were applied in the searches.

CASE

A 30-year-old pregnant woman (weight 63 kg, BMI 23) of Romanian descent was scheduled for an elective cesarean section at 38 weeks of gestation. The patient had suffered three MS relapses, respectively 16 years, 12 years and 15 months ago. She was diagnosed with relapsing-remitting MS after the second relapse. Symptoms during these relapses ranged from paresis of the lower left leg, during the first two exacerbations, to quadriparesis and severe ataxic gait during the last attack. Fortunately, full recovery without sequelae was obtained after each event. Subsequent MRI revealed white matter lesions within the spinal cord at T8 and T10. Between the second and third relapse no new lesions were discovered on MRI. No pharmacological therapy was administered or started in this period. After the third relapse, 15 months ago, new MRI lesions were revealed between the second and third cervical vertebra. High doses methylprednisolone were administered resulting in good recovery. Two months later an interferon-based treatment was started as well, which was discontinued after another five months, once pregnancy was confirmed.

During three months following delivery, no MS related pharmacological therapy was administered or restarted. Apart from MS, the patient suffered from a persistent Generalized Anxiety Disorder for which behavioral therapy was attended. This therapy, however, only slightly alleviated the psychological symptoms.

Six years earlier, she gave birth to a son through an uneventful cesarean section under general anesthesia. At that time, general anesthesia was preferred because of the existing needle phobia and intense fear of potential witnessing the anesthetic and surgical procedure.

A profound neurological and general clinical examination, at the moment of admission to the hospital for elective cesarean section, could not withhold any abnormalities. Respiratory and autonomic nervous system were found to be normal and had never been affected during exacerbations. Laboratory results (complete blood count, coagulation testing, electrolytes, kidney- and liver function tests) were normal at the moment of admission.

Even though, for the reasons stated above, general anesthesia was chosen for the first cesarean section, this may not be the safest option as general anesthesia is known to carry important risks for mother and baby, notably airway management problems and aspiration pneumonia (10). Furthermore, important postoperative respiratory complications, after emergence from general anesthesia, may arise if MS lesions affect the respiratory centers in the medulla oblongata (11). General anesthetics are also known to have immune suppressing effects, which could possibly influence the course of MS (12, 13).

Bearing in mind these risks, the patient was carefully informed about the different anesthetic possibilities. After careful deliberation, epidural anesthesia was rejected, as the patient expressed profound fear of the idea of an indwelling epidural catheter, and spinal anesthesia was preferred. In addition the patient was informed about the increased risk of relapse in the post-partum period. Eventually, the informed consent was obtained. Standard monitoring was applied for the procedure (electrocardiogram, heart rate and blood pressure monitoring and pulse oximetry).

Spinal anesthesia was executed in sitting position, using a 27 gauge Whitacre needle, between the fourth and fifth lumbar level. A 2 ml mixture containing 2 µg sufentanil and 8 mg hyperbaric bupivacaine was administered in the subarachnoid space. A sensory block rose to T4 within 10 minutes. A motor block, graded 4 on the Bromage scale (grade 1: free movement of knees and feet, grade 2: limited ability to flex knees with free movement of feet, grade 3: unable to flex knees with free movement of feet, grade 4: unable to move knees or feet), was objectified a few minutes later (14). No additional analgesia was needed during the procedure. The motor block fully recovered after 2 hours and 20 minutes, whilst the sensory block lasted for approximately 5 hours. Systolic blood pressure ranged between 95 and 125 mmHg throughout the procedure. Three bolus injections of 0.1 mg phenylephrine were administered to counter hypotension. No significant episodes of hypotension or bradycardia were seen per- or post-operatively. The temperature was stable around 36.5 degrees Celsius. VAS-scores during surgery never exceeded 1/10. Four, 12 and 24 hours after surgery VAS-scores were respectively 1, 3 and 2. Postoperative analgesia consisted of an oral oxycodone scheme.

Postoperative laboratory results were within normal limits. Neurologic examination 24 hours,

72 hours (just before discharge) and 3 months after cesarean section could not detect any abnormalities or relapses. No MRI was performed during the 3-month follow-up period.

DISCUSSION AND LITERATURE REVIEW

It is widely accepted that regional anesthesia is safer than general anesthesia for cesarean section (15). A higher probability to encounter a difficult airway, aspiration risk and the mandatory rapid sequence induction all lead to higher morbidity and mortality in the obstetric population. These risks have to be taken into account in the anesthetic decision making process.

Anesthetic management in the MS patient, especially in the setting of delivery, is even more challenging. Despite some inexplicit recommendations by the advisory board of the American Society of Regional Anesthesia and Pain Medicine (ASRA) (16), clear guidelines are lacking. For decennia, neuraxial anesthesia in MS patients faced widespread skepticism due to concerns of disease aggravation. This mistrust is caused by several factors. Firstly, the post-partum period (three months following delivery) has been identified as a separate risk factor for MS exacerbation or relapse (5, 17). Pregnancy, on the other hand, protects against MS exacerbations. This is due to a shift from cellular mediated immunity to humoral mediated immunity during pregnancy. A contrariwise shift after delivery contributes to the increased relapse rate in the post-partum period (18). As most research has been executed in the setting of delivery, a falsely high incidence of MS exacerbations was seen in some historical case reports and case series (19). This improper causality is due to ignorance of the post-partum period as a separate risk factor and likely contributed to initial skepticism concerning the safe use of neuraxial anesthesia in patients with MS.

Secondly, theoretical concerns have been postulated as well. One such concern is based on the double crush theory, as first described by Upton and McComas in 1973 (20). It suggests that neurons with pre-existing damage (such as demyelination) are more susceptible for distal denervation after a minor neural event somewhere along the affected neural pathway. It has frequently been postulated that neuraxial anesthesia could fit the role of a second hit in patients with MS due to the potential mechanical trauma, anesthetic local toxicity or neural ischemia through additives (21).

Another theoretical consideration is the purported presence of abnormal high concentrations

of certain oligopeptides in the cerebrospinal fluid of MS patients (22). Among those oligopeptides, some have been reported to exert a sodium-channel blocking activity. This is supposed to lead to a partial conduction block in demyelinated axons causing MS symptoms (23, 24). The structure of local anesthetics resembles the structure of the sodium-channel-blocking oligopeptides, and it has been shown that lidocaine, when given intravenously, can trigger transient and reversible MS symptoms. Through their sodium-channel blocking activity, local anesthetic drugs could increase the amplitude of a conduction block in silent demyelinated axons which may lead to transient MS symptoms (25). In neuraxial anesthesia, especially spinal anesthesia, local anesthetics reach the intrathecal space where they could 'unmask' previously silent demyelinated plaques through the same mechanism (26). These effects caused by systemically or intrathecally administered local anesthetics are thought to be transient and reversible and will not cause an aggravation of the underlying condition (21). This transient effect however, is an additional reason why different reports in the past associated spinal anesthesia with disease exacerbation (27-29). Clearly, more recent clinically oriented studies have failed to show a correlation between neuraxial anesthesia and MS exacerbation (21, 30). In view of the purported neurotoxic effects of local anesthetics (21, 31, 32), it is advisable to use the lowest local anesthetic dose possible when opting for a neuraxial technique (33). Logically, when opting for an epidural technique, less local anesthetics will reach the intrathecal space in comparison to a spinal technique. Hence an epidural anesthesia could be preferred to spinal anesthesia (21, 31).

At present, sufficient evidence for safe administration of epidural anesthesia is available in patients with MS. One of the only prospective large trials to date was conducted by Confavreux and colleagues (5). In this study, 241 patients with MS were followed of whom 42 received an epidural anesthesia. No correlation was found between epidural anesthesia for delivery and disease exacerbation. An Italian cohort study, including pregnancies between 2002 and 2008 in women with MS, elaborated on the follow-up of 155 patients with cesarean section delivery, of whom 65 underwent epidural anesthesia (34). Multivariate analysis could not demonstrate an increased risk of post-partum relapses in the epidural versus the general anesthesia group. A more recent Portuguese retrospective cohort circumscribed similar results (35). Between 1993 and 2015, 111 MS pregnancies

were followed and examined, of which 62 patients received epidural anesthesia. Again, multivariate analysis could not associate epidural anesthesia with an increased risk for post-partum relapse.

Evidence for spinal anesthesia is less abundant. Nevertheless, recent literature is fairly convincing that spinal anesthesia is safely applicable as well. In the 1990's, several case reports, such as the one by Martucci *et al.*, reported the safe administration of spinal anesthesia for elective cesarean section in a patient with MS (36). No neurologic complications were seen during a 12-month follow-up. In a retrospective case series, by Bouchard and colleagues, 14 patients with MS were given a spinal anesthesia for small urologic procedures (37). Except for one case who presented with transient MS symptoms, no disease exacerbation or aggravation of disease was withheld. Hebl *et al.* concluded on the basis of a large retrospective cohort study that neither spinal, nor epidural anesthesia contributed to disease relapse or aggravation (38). In 2013, a paper based on the British Columbia MS database (1998-2009) demonstrated that the Expanded Disability Status scale – an internationally recognized measure for disease disability and progression of MS – was not associated with the use of either epidural (n=116) nor spinal anesthesia (n = 82) (39). Another retrospective cohort study by Harazim *et al.* followed 70 deliveries in MS patients from which 25 patients required cesarean section (40). Despite the fact that only one patient received spinal anesthesia, the authors concluded based on their secondary outcome results that the type of obstetric anesthesia, until 6 months after delivery, did not influence the course of MS.

Additionally, it is worth noting that MS patients are more inclined to develop hypotension, bradycardia and cardiac arrhythmias as a consequence of (a possible) autonomic nervous system dysfunction. Moreover, vasopressor therapy will be less effective in treating episodes of hypotension in the MS population (41). An in-depth preoperative examination of the autonomic nervous system and a pre-operative electrocardiography are therefore warranted. Special attention should be given to hemodynamic monitoring during cesarean section (42). Due to the acceptable safety profile of neuraxial anesthesia in MS patients nowadays, a spinal technique and even more an epidural anesthesia, are considered the better anesthetic options in the obstetric MS population (10, 32). In a recent survey among obstetric anesthesiologists, more than 90% would opt for a spinal anesthesia for emergency cesarean section in patients with MS when time

for an epidural anesthesia is lacking. According to this survey, spinal anesthesia is a valuable option for an emergency cesarean section in the obstetric MS population, in order to avoid the risks of general anesthesia (43). In an elective cesarean section, epidural anesthesia is mostly the better choice for analgesia. But for emergency cesarean section or in certain cases, a spinal anesthesia could be a valuable option. In the present case spinal anesthesia seemed the most appropriate option given the patient's General Anxious Disorder and needle phobia.

CONCLUSION

Nowadays, neuraxial anesthesia is no longer contra-indicated in patients with MS. For purely theoretical reasons epidural anesthesia is still considered the safer choice, but clinical studies over the last decade have shown spinal anesthesia to be an appropriate option. The anesthesia conduct in this case report illustrates the latest consensus regarding the safety of spinal anesthesia in patients with MS undergoing cesarean section. The decision which anesthesia technique will be used, should be patient-tailored and should be thoroughly discussed with the patient, and informed consent must be obtained. Detailed pre-operative examination and informed consent plays an important part in the decision-making process.

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